PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PN03101-PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/NO2004/000389	International filing date *(day/month/year)* 16.12.2004	Priority date *(day/month/year)* 19.12.2003
International Patent Classification (IPC) or national classification and IPC INV. C07D265/32		
Applicant AMERSHAM HEALTH AS		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10.10.2005	12.05.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bakboord, J Telephone No. +49 89 2399-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NO2004/000389

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-10 as originally filed

   Claims, Numbers

   1-17 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	17
Inventive step (IS)	Yes:	Claims	1-16
	No:	Claims	17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The present invention relates to a process for the production of diethylenetriaminepentaacetic acid-bis(anhydride) (DTPA-bis(anhydride)).

V.2 Reference is made to the following documents:

D1: EP-A-0 183 760, cited in the application
D2: US-A-3 660 388, cited in the application
D3: US-A-5 508 388, cited in the application
D4: US-A-4 707 453, cited in the application
D5: US-A-4 822 594, cited in the application
D6: US-A-4 698 263, cited in the application
D7: MIYAMOTO M ET AL: "DESIGN AND PREPARATION OF GADOLINIUM-RESERVOIR MICROCAPSULES FOR NEUTRON-CAPTURE THERAPY BY MEANS OF THE WURSTER PROCESS" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol. 45, no. 12, December 1997 (1997-12), pages 2043-2050, XP000731370 ISSN: 0009-2363
D8: ECKELMAN W C ET AL: "NEW COMPOUNDS: FATTY ACID AND LONG CHAIN HYDROCARBON DERIVATIVES CONTAINING A STRONG CHELATING AGENT" JOURNAL OF PHARMACEUTICAL SCIENCES, AMERICAN PHARMACEUTICAL ASSOCIATION. WASHINGTON, US, vol. 64, no. 4, April 1975 (1975-04), pages 704-706, XP002055770 ISSN: 0022-3549

V.3 Novelty

Documents D1, D2, D4-D8 all disclose a process for the production of (DTPA-bis(anhydride) from DTPA, acetic acid anhydride and pyridine. The amount of pyridine in each of the cases is above 6 moles per mole DTPA.
Document D3 discloses a process for the production of (DTPA-bis(anhydride) from DTPA, acetic acid anhydride, pyridine and acetonitrile.

A process for the production of (DTPA-bis(anhydride) from DTPA, acetic acid and pyridine in which the amount of pyridine is equal or less than 6 times the molar amount of DTPA is disclosed in none of the documents. Claims 1-16 therefore fulfill the requirements of Art 33(2) PCT.

DTPA-bis(anhydride) is disclosed in documents D1-D8. The fact that it is produced by a novel synthesis does not render the compound novel. Claim 17 therefore does not fulfill the requirements of Art 33(2) PCT.

V.4 Inventive step

Starting from documents D1-D8 the problem to be solved by the present application may be regarded as how to provide a novel possibly improved synthesis for (DTPA-bis(anhydride). The solution of the applicant resides in providing a process in which the amount of pyridine is less than the amounts used in the prior art. In document D3 the amount of pyridine is also less than 6 molar equivalents however acetonitrile is used in that reaction. The applicant shows in table 1 that it is possible to perform the reaction with low pyridine concentrations resulting in (DTPA-bis(anhydride) with good purity. As nowhere it is stated in the prior art that the reaction can be performed using less pyridine which is toxic and relatively expensive the solution of the applicant may be regarded as involving an inventive step (Art 33(3) PCT).